Appl. No. 09/834,760 Amdt. dated June 30, 2004 Reply to Office Action of December 31, 2003

<u>Amendments to the Claims:</u> This listing of claims will replace all prior versions, and listings of claims in the application:

## **Listing of Claims:**

Claims 1-17 (canceled)

1	Claim 18 (withdrawn): A method of preventing or treating a thrombotic disease
2	or condition in a mammal, the method comprising producing an ER resident chaperone protein
3	within a population of cells of said mammal, whereby the generation of active thrombin on the
4	surface of said population of cells is inhibited.
1 2	Claim 19 (withdrawn): The method of claim 18, wherein said population of cells comprises endothelial cells.
1	Claim 20 (withdrawn): The method of claim 18, wherein said population of cells
2	comprises smooth muscle cells.
1	Claim 21 (withdrawn): The method of claim 18, wherein said population of cells
2	comprises macrophages.
1	Claim 22 (withdrawn): The method of claim 18, wherein said population of cells
2	comprises monocytes.
1	Claim 23 (withdrawn): The method of claim 18, wherein said ER resident
2	chaperone protein is GRP78/BiP.
1	Claim 24 (withdrawn): The method of claim 18, wherein said ER resident
2	chaperone protein is selected from the group consisting of GRP94, GRP72, Calreticulin,
3	Calnexin, Protein disulfide isomerase, cis/trans-Prolyl isomerase, and HSP47.

Appl. No. 09/834,760 Amdt. dated June 30, 2004 Reply to Office Action of December 31, 2003

1	Claim 25 (withdrawn): The method of claim 18, wherein the production of said
2	ER resident chaperone protein within said population of cells results in a decrease in the level of
3	tissue factor procoagulant activity on the surface of said population of cells.
1	Claim 26 (withdrawn): The method of claim 18, wherein said population of cells
2	is present within an atherosclerotic plaque in said mammal.
1	Claim 27 (withdrawn): The method of claim 18, wherein said mammal has had a
2	myocardial infarction and is undergoing angioplasty or stenting.
1	Claim 28 (withdrawn): The method of claim 27, wherein said mammal is
2	undergoing stenting, and said population of cells is present on the surface of a stent within said
3	mammal.
1	Claim 29 (withdrawn): The method of claim 18, wherein said mammal is
2	undergoing cranial radiation.
1	Claim 30 (withdrawn): The method of claim 18, wherein said mammal is
2	undergoing vascular surgery.
1	Claim 31 (withdrawn): The method of claim 18, wherein a polynucleotide
2	encoding said ER resident chaperone protein, operably linked to a promoter, is introduced into
3	said population of cells, whereby said ER resident chaperone protein is produced.
1	Claim 32 (withdrawn): The method of claim 31, wherein said polynucleotide is
2	introduced into said cell using a viral vector.
1	Claim 33 (withdrawn): The method of claim 32, wherein said viral vector is an
2	adenoviral vector.

1	Claim 34 (withdrawn): The method of claim 31, wherein said polynucleotide is
2	introduced into said cell using a nonviral vector.
1	Claim 35 (withdrawn): The method of claim 34, wherein said nonviral vector is
2	introduced into said cell as naked DNA or using liposome-mediated transfection.
l	Claim 36 (withdrawn): The method of claim 18, wherein said ER resident
2	chaperone protein is produced by administering to said population of cells a compound that
3	induces the expression or activation of an endogenous ER resident chaperone protein.
)	induces the expression of activation of an endogenous ER resident enaperone protein.
1	Claim 37 (withdrawn): The method of claim 36, wherein said compound is a
2	cytokine.
l	Claim 38 (withdrawn): A method of identifying a compound that is useful in the
2	treatment or prevention of a thrombotic disease or condition, the method comprising:
3	(1) contacting a cell that expresses an ER resident chaperone protein, or that is
4	capable of expressing an ER resident chaperone protein, with said compound; and
5	(2) detecting the functional effect of said compound on said ER resident
5	chaperone protein;
7	wherein an increase in the expression or activity of said ER resident chaperone
3	protein in said cell indicates that said compound would be useful in the treatment or prevention
9 .	of said thrombotic disease or condition.
1	Claim 39 (withdrawn): The method of claim 38, wherein said ER resident
2	chaperone protein is GRP78/BiP.
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1	Claim 40 (withdrawn): The method of claim 38, wherein said ER resident
2	chaperone protein is selected from the group consisting of GRP94, GRP72, Calreticulin,
3	Calnexin, Protein disulfide isomerase, cis/trans-Prolyl isomerase, and HSP47.

Appl. No. 09/834,760 Amdt. dated June 30, 2004 Reply to Office Action of December 31, 2003

1	Claim 41 (withdrawn): The method of claim 38, wherein said cell is an
2	endothelial cell.
1	Claim 42 (withdrawn): The method of claim 38, wherein said cell is a smooth
2	muscle cell.
1	Claim 43 (withdrawn): The method of claim 38, wherein said cell is a
2	macrophage.
1	Claim 44 (withdrawn): The method of claim 38, wherein said cell is a monocyte.
1	Claim 45 (withdrawn): The method of claim 38, wherein said compound induces
2	said expression or activation of said ER resident chaperone protein in said cell without inducing
3	ER stress in said cell.
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1	Claim 46 (withdrawn): A method of treating or preventing a thrombotic disease
2	in a mammal, the method comprising administering to said mammal a therapeutically or
3	prophylactically effective amount of a compound identified using the method of claim 38.
1	Claim 47 (currently amended) A method of inhibiting the generation of active
2	thrombin on the surface of a cell within an atherosclerotic plaque within a mammal, the method
3	comprising increasing the expression or activity of an ER resident calcium-binding protein in
4	said cell by introducing a polynucleotide operably linked to a promoter into said cell, wherein
5	said polynucleotide encodes said ER resident calcium-binding protein producing an ER
6	resident-chaperone protein in said cell within an atheroselerotic plaque within said
7	mammal.
1	Claim 48 (previously presented) The method of claim 47, wherein said cell is an
2	endothelial cell.
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Appl. No. 09/834,760 Amdt. dated August 27, 2003 Reply to Office Action of December 31, 2003

1	Claim 49 (previously presented): The method of claim 47, wherein said cell is a
2	smooth muscle cell.
1	Claim 50 (previously presented): The method of claim 47, wherein said cell is a
2	macrophage.
1	Claim 51 (previously presented): The method of claim 47, wherein said cell is a
2	monocyte.
1	Claim 52 (currently amended): The method of claim 47, wherein said ER
2	resident <u>calcium-binding</u> ehaperone protein is GRP78/BiP.
1	Claim 53 (currently amended): The method of claim 47, wherein said ER
2	resident calcium-binding chaperone protein is selected from the group consisting of GRP94,
3	GRP72, Calreticulin, Calnexin, Reticulocalbin, Protein disulfide isomerase, cis/trans-Prolyl
4	isomerase, and HSP47.
1	Claim 54 (currently amended): The method of claim 47, wherein the <u>increase in</u>
2	the expression or activity production of said ER resident calcium-binding chaperone protein
3	within said cell results in a decrease in the level of tissue factor procoagulant activity on the
4	surface of said cell.
	Claim 55 (canceled
1	Claim 56 (currently amended): The method of claim 47 55, wherein said
2	polynucleotide is introduced into said cell using a viral vector.
1	Claim 57 (previously presented): The method of claim 56, wherein said viral
2	vector is an adenoviral vector.

Appl. No. 09/834,760 Amdt. dated August 27, 2003 Reply to Office Action of December 31, 2003

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cytokine is interleukin-3.

1	Claim 58 (currently amended): The method of claim 47 55, wherein said
2	polynucleotide is introduced into said cell using a nonviral vector.
1	Claim 59 (previously presented): The method of claim 58, wherein said nonviral
2	vector is introduced into said cell as naked DNA or using liposome-mediated transfection.
	Claims 60-61 (canceled)
1	Claim 62 (currently amended): A method of inhibiting the generation of active
2	thrombin on the surface of a cell within a mammal, the method comprising increasing the
3	expression or activity of an ER resident calcium-binding protein in said cell by administering a
4	proinflammatory cytokine to said cell producing an ER resident chaperone protein in said
5	eell within said mammal by introducing into said cell a polynucleotide operably linked to a
6	promoter, wherein said polynucleotide encodes said ER resident chaperone protein,
7	whereby said-ER resident chaperone protein is produced.
	Claims 63-66 (canceled)

Claim 67 (new): The method of claim 62, wherein said proinflammatory